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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/438,206	11/12/1999	RIYI SHI	7024-427-PUR	9018

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EXAMINER	
HUI, SAN MING R	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 01/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/438,206	SHI ET AL.	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 November 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-30,38-40,43 and 44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-30, 38-40, 43, and 44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

Applicant's amendments filed November 15, 2002 have been entered.

The addition of claim 44 in amendments filed November 15, 2002 is acknowledged. The cancellation of claims 31-37, 41 and 42 in the amendments filed March 5, 2002 is acknowledged.

Claims 22-30, 38-40, 43, and 44 are pending.

The outstanding rejection under 35 USC 112, second paragraph regarding "compound action potential" is withdrawn in view of the amendments in the claims filed November 15, 2002.

Upon reconsideration, the rejections of claims 23 and 24 under 35 USC 103 are withdrawn because of the nature of the injury caused by severing or crushing the spinal cord would be different than that of compressing the spinal cord.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 30 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment employing the synergistic combination of polyethylene glycol (PEG) and 4-aminopyridine (4-AP), does not reasonably provide enablement for combination of C_3-C_{10} polyalkylene glycols and other potassium channel blockers.

In the instant case, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art

7) the predictability of the art, and

8) the breadth of the claims.

Applicant fails to set forth the criteria that define the useful combination of "C_3-C_{10} polyalkylene glycols" and "potassium channel blockers". Additionally, Applicant fails to provide information allowing the skilled artisan to ascertain these compounds without undue experimentation. In the instant case, the only example set forth is the synergistic combination of "PEG and 4-AP", thereby failing to provide sufficient working examples. It is noted that these examples are neither exhaustive, nor define the combination of

compounds required. Synergistic effect is unpredictable, requiring each embodiment to be individually assessed for physiological activity. The instant claims read on **all** "potassium channel blockers", necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 30 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation "said method resulting in a synergistic increase... behavior in said patient." in claim 30, lines 4-6 renders the claims indefinite as to method steps required to achieve the recited results. It is not clear what amount of potassium channel blockers would exhibit synergistic activities with polyalkylene glycol.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 22, 25-29, 38-39 are rejected under 35 U.S.C. 102(b) as being anticipated by Davis et al. (Journal of Spinal Disorders, 1990;3(4):299-306).

Davis et al. teaches that Depo-Medrol, a depot formulation of methylprednisolone containing PEG 3350 (the product information of Depo-Medrol from PDR, 1996, page 2600-2602 is also provided), is instilled to patients having an exposed nerve root during a spinal lumbar surgery for disc excision and retraction of the nerve root with incision (See particularly the abstract). Davis et al. further teaches this procedure leads to a condition of reduced pain and spasm (See the abstract; and page 300, col. 2, last paragraph), which indicates that the patients' behavioral and neural functions are restored. Davis et al. also teaches Ciembroniewicz applying Depo-Medrol epidurally to patients at lumbar surgery for disc excision (See page 300, col. 1, third paragraph). The claims now recite the limitations of "a method of treating a patient suffered a spinal cord injury with C_1-C_{10} polyalkylene glycol".

Applicants' attention is directed to *Ex parte Novitski*, 26 USPQ2d 1389 (BOPA 1993) illustrating anticipation resulting from inherent use, absent a *haec verba* recitation for such utility. In the instant application, as in *Ex parte Novitski*, supra, the claims are directed to treating a mammalian patient suffered an injury to its spinal cord with polyethylene glycol. It is now well-settled law that administering compounds inherently possessing a protective utility anticipates claims directed to such protective use. Arguments that such protective use is not set forth *haec verba* are not probative. Prior use for the same utility clearly anticipates such utility, absent limitations distancing the proffered claims from the inherent anticipated use. Attempts to distance claims from

anticipated utilities with specification limitations will not be successful. At page 1391, *Ex parte Novitski*, supra, the Board said "We are mindful that, during the patent examination, pending claims must be interpreted as broadly as their terms reasonably allow. *In re Zletz*, 893 F.2d 319, 13 USPQ2d 1320 (Fed. Cir. 1989). As often stated by the CCPA, "we will not read into claims in pending applications limitations from the specification." *In re Winkhaus*, 52 F.2d 637, 188 USPQ 219 (CCPA 1975).". In the instant application, Applicants' failure to distance the proffered claims from the anticipated prophylactic utility, renders such claims anticipated by the prior inherent use.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 22, 30-37, 40, and 43-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Davis et al. (Journal of Spinal Disorders, 1990;3(4):299-306) in view of Potter et al. (Clin Invest Med, 19(4), Suppl.: S80, #533), references of record in the previous office action mailed November 23, 2001.

Davis et al. teaches that Depo-Medrol, a depot formulation of methylprednisolone containing PEG 3350 (the product information of Depo-Medrol from PDR, 1996, page 2600-2602 is also provided), is instilled into patients having an exposed nerve root during a spinal lumbar surgery for disc excision and retraction of the nerve root with

incision (See particularly the abstract). Davis et al. further teaches that the procedure leads to a condition of reduced pain and spasm (See the abstract; and page 300, col. 2, last paragraph), which indicates that the patients' behavioral and neural functions are restored. Davis et al. also teaches Ciembroniewicz applying Depo-Medrol epidurally to patients at lumbar surgery for disc excision (See page 300, col. 1, third paragraph). The claims now recite the limitations of "a method of treating a patient suffered a spinal cord injury with C_1-C_{10} polyalkylene glycol".

Davis et al. does not expressly teach 4-aminopyridine, the potassium channel blocker, can be combined with method of Davis et al. to treat patients with spinal cord injury.

However, Potter et al. teaches the use of 4-aminopyridine to treat spinal cord injury (See #533).

It would have been obvious to one skill in the art when the invention was made to employ a combination of 4-aminopyridine with polyethylene glycols to treat mammalian patients with spinal cord injury.

One of ordinary skill in the art would have motivated to employ a combination of 4-aminopyridine with polyethylene glycols to treat mammalian patients with spinal cord injury including crushing or severing injuries, because combining two agents which are known to be useful to treat spinal cord injury individually into a single method that is useful for the very same purpose is prima facie obvious. See *In re Kerkhoven* 205 USPQ 1069. At least additive therapeutic effects are reasonably expected.

Allowable subject matter

Claims 23-24 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The method of treating severed or crushed spinal cord injury, as recited in claims 23 and 24, is not taught or fairly suggested by the prior art.

Response to the arguments directed to rejections under 35 USC 102(b) and 103(a)

Since Applicant's arguments filed November 15, 2002 are applicable to rejections under both 35 USC 102 and 103, they are addressed together below.

Applicant's rebuttal arguments filed November 15, 2002 averring the amended claims are now directed to the proper surgical procedure will not cause spinal cord injury have been considered, but are not found persuasive. Injury to the spinal cord can be in the form of a contusion or compression of the spinal cord (See instant specification, page 14, lines 21-24). Compression of the spinal cord can be caused by various reasons, such as infections, broken vertebra or other bone in the spinal column, a rupture of one or more of the cartilage disks that lie between the veterbrae, or a tumor that press against the spinal cord (See Merck Manual of Medical Information – Home Edition, 1997, page 352-353). Patients undergoing disc excision surgery would be suffered from compression to their spinal cord because bones in the vertebrae column and the cartilage disks are removed. Depo-Medrol, a PEG containing composition, was

administered epidurally to the patient, after the traumatic event, i.e., the moment of the disc being excised (but still during the surgery), to reduce the pain and spasm.

Applicant's rebuttal arguments filed November 15, 2002 averring the result of recovery of the conductance functions of the spinal cord have been considered, but are not found persuasive. These effects, i.e., restoration of the neural functions, are considered as inherent result from the epidural administering the polyethylene glycol containing composition.

It is apparently the claims herein are encompassing some other forms of spinal cord injuries that are beyond what the inventors envisioned.

See also the discussion in response to Dr. Shapiro's declarations below.

Response to the declaration by Dr. Shapiro

Dr. Shapiro's statement in declaration filed November 15, 2002 are directed to the surgical procedure to remove the disks will not result in spinal cord injury have been considered, but are not found persuasive. The surgical procedure may not directly cause the injury to the spinal cord, nevertheless, the result of removing the bones inorder to remove the disk, results in spinal cord compression. Merck Manual of Medical Information – Home Edition, 1997, page 352-353, a basic medical reference one of ordinary skill in the art charged to know, teaches that spinal cord compression can be caused by various reasons, such as infections, broken vertebra or other bone in the spinal column, a rupture of one or more of the cartilage disks that lie between the veterbrae, or a tumor that press against the spinal cord. In Benzel, page 391, col. 2,

third paragraph and page 392, Fig. 28.1, teaches that removal of various bones are necessarily prior to removing the disk from the vertebrae. In view of the cited references, removing the bone from the vertebrae would cause spinal cord compression. Since the polyethylene glycol containing composition is administered epidurally in patients during the discectomy surgery, the claims are anticipated and rendered obvious by the cited prior art. It is apparently the claims herein are encompassing some other forms of spinal cord injuries that are beyond what the inventors envisioned.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-

1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (703) 305-1877. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

San-ming Hui
January 24, 2003

SREENI PADMANABHAN
PRIMARY EXAMINER

1/27/03